L5 ANSWER 1 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93096969 EMBASE
DOCUMENT NUMBER: 1993096969
TITLE: Angiogenesis, neovascular proliferation and vascular pathophysiology as targets for **cancer** therapy.
AUTHOR: **Denekamp J.**
CORPORATE SOURCE: CRC Gray Laboratory, Mount Vernon Hospital, PO Box 100,Northwood, Middlesex HA6 2JR, United Kingdom
SOURCE: British Journal of Radiology, (1993) 66/783 (181-196). ISSN: 0007-1285 CODEN: BJRAAP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A body of evidence that vascular-mediated damage occurs in murine tumours after many existing forms of anti-tumour therapy is rapidly accumulating. Rapid conventional screens of cells in vitro or using leukaemias of lymphomas will not detect this mode of action and such screens will therefore miss effective agents. A change in the approach to experimental **cancer** therapy is needed to ensure that this important new avenue is fully investigated. Solid tumours will need to be studied and the importance of specific tumour cell biochemistry (e.g. on tissue factor procoagulant activity), of **endothelial** status and the immunocompetence of the host are all likely to be important. It is a subject of considerable debate at present whether transplanted subcutaneous mouse tumours are adequate models and whether they will reflect the response of spontaneous tumours, or even of transplants into other sites. Xenografts are not likely to be appropriate if the immuno-suppressed hosts lack the cells needed for the cytokine component of the pathway. The strategy of design and screening of new agents, for scheduling of existing agents and particularly the sequencing of adjunctive therapies are likely to be completely different for the 'direct' tumour cell or 'indirect' vascular-mediated approaches. It may eventually be appropriate to combine vascular manipulation with direct cytotoxicity aimed at malignant cells but the two mechanisms must be recongized as distinct entities and considered separately before attempting to coordinate them. It is important therefore to identify the 'hallmarks' of vascular mediated injury and the means by which this can be distinguished from direct cell kill. These may be detectable in the tumour response but clues can also be gained from the side effects that are seen in normal tissues both with existing and with novel therapies. The appeal of vascular-mediated ischaemic therapy is that it is systemic and will have the potential of being effective on any tumour with a newly evoked vascular network, i.e. of about 1 mm in diameter, but it will be even more effective on large tumours than on small. Thus it should affect both large primary tumours and disseminated small metastases. The studies with many different anti-**cancer** agents have illustrated the potential complexity of responses that can appear to cause tumour cell death by collapse or occlusion of the blood supply. They have also focused

attention on features of disparate agents, e.g. TNF, FAA, PDT, which may share similar pathways. No single feature of neovasculature can be highlighted as the sole route by which such antivascular therapy should be targeted. Rapid proliferation of the **endothelial** cells may prove to be a target, but it also influences differentiation characteristics, so that the immature cells will function abnormally. The permeability of these poorly formed vessels may lead to extravasation of proteins leading to increased interstitial pressures and by this means to an imbalance between intravascular and extravascular pressures and hence to collapse of the thin-walled vessels. Changes in systemic blood pressure, cardiac output, viscosity or coagulation and especially a redistribution of regional perfusion would all have differential effects in tumours and normal vessels. Clearly both vascular patho-physiology and the complexity of **endothelial** cell function and its imbalance in neovasculature will be important in understanding the mechanism of action of antivascular strategies. This very challenging boundary between oncology and a number of other medical and biological fields promises to lead to altered attitudes to existing therapies and the discovery of completely new classes of anti-**cancer** agents. The next decade should translate into clinical benefit for patients if the progress in this field continues to be as rapid as it has been in the late eighties. We must now determine what characteristics make one tumour more sensitive than another to agents such as heat, PDT, cytokines and FAA, and learn how to extrapolate from those rodent tumours to the human.

TI Angiogenesis, neovascular proliferation and vascular pathophysiology as targets for **cancer** therapy.

AU **Denekamp J.**

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CT Medical Descriptors:
*angiogenesis
***cancer therapy**
*radiosensitization
*tumor vascularization
animal cell

animal experiment
animal model
antineoplastic activity
cancer chemotherapy
cancer radiotherapy
cartilage
cell kinetics
dna synthesis
drug cytotoxicity
endothelium cell
human
hyperthermic therapy
hypotension: SI, side effect
hypoxia
melanoma: DT, drug therapy
nonhuman
photodynamic therapy
priority journal
radiation dose fractionation
radiation protection
radiosensitivity
rat
review
thrombocyte aggregation
topical drug administration
tumor. . .

L5 ANSWER 2 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90389713 EMBASE
DOCUMENT NUMBER: 1990389713
TITLE: Vascular attack as a therapeutic strategy for **cancer.**
AUTHOR: **Denekamp J.**
CORPORATE SOURCE: CRC Gray Laboratory, Mount Vernon Hospital, P.O. Box 100,Northwood HA6 2JR, United Kingdom
SOURCE: Cancer and Metastasis Reviews, (1990) 9/3 (267-282). ISSN: 0167-7659 CODEN: CMRED4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The blood supply to all solid tumours consists of the parasitized normal vessels and new vessels which have been induced to grow by the presence of the tumour. These vessels are inadequate in many respects, being tortuous, thin-walled, chaotically arranged, lacking innervation and with no predetermined direction of flow. The walls consist of a basement membrane lined with rapidly proliferating immature **endothelial** cells, and are more permeable than normal vessels. The spacing of the vessels and their average diameters are not optimal for nutrient provision. This paper focuses on the evidence that many existing therapies may already have, as part of their action, a vascular mediated process of killing tumour cells. This may result from local changes within individual vessels or from systemic alterations in blood pressure, viscosity, coagulability etc. The hallmarks of vascular injury are identified and the dangers of discarding useful anticancer agents by failing to understand their mechanism of action are highlighted.
TI Vascular attack as a therapeutic strategy for **cancer.**
AU **Denekamp J.**
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immature **endothelial** cells, and are more permeable than normal vessels. The spacing of the vessels and their average diameters are not optimal. . .

CT Medical Descriptors:
***cancer chemotherapy**
*cell growth
*endothelium cell
*tumor blood flow
cytochemistry
human
nonhuman
article
priority journal
*antineoplastic agent: PD, pharmacology
*antineoplastic agent: CB, drug combination
*cytokine: PD, pharmacology
*mitoflaxone: PD, pharmacology
*mitoflaxone: DO, drug. . .

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ISSN: 0167-7659 CODEN: CMRED4
CY Netherlands
DT Journal; Article
FS 016 Cancer
037 Drug Literature Index
LA English
SL English

L5 ANSWER 3 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85172794 EMBASE
DN 1985172794
TI Vascular endothelium as the vulnerable element in tumours.
AU **Denekamp J.**
CS Gray Laboratory of the Cancer Research Campaign, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom
SO Acta Radiologica Oncology, (1984) 23/4 (217-225).
CODEN: AROBDR
CY Sweden
DT Journal
FS 014 Radiology
016 Cancer
023 Nuclear Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English

L5 ANSWER 4 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 83108716 EMBASE
DN 1983108716
TI Vascular occlusion and tumour cell death.
AU **Denekamp J.**; Hill S.A.; Hobson B.
CS Gray Lab., Cancer Res. Camp., Mt. Vernon Hosp., Northwood, Middlesex HA6

2RN, United Kingdom
SO European Journal of Cancer and Clinical Oncology, (1983) 19/2 (271-275).
CODEN: EJCAAH
CY United Kingdom
DT Journal
FS 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
005 General Pathology and Pathological Anatomy
LA English

L5 ANSWER 5 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 83038262 EMBASE
DN 1983038262
TI **Endothelial**-cell proliferation in experimental tumours.
AU **Denekamp J.**; Hobson B.
CS Gray Lab., Cancer Res. Camp., Mt. Vernon Hosp., Northwood, Middlesex HA6 2RN, United Kingdom
SO British Journal of Cancer, (1982) 46/5 (711-720).
CODEN: BJCAAI
CY United Kingdom
DT Journal
FS 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
005 General Pathology and Pathological Anatomy
LA English

L5 ANSWER 6 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82123547 EMBASE
DN 1982123547
TI Proliferation kinetics of **endothelial** and tumour cells in three mouse mammary carcinomas.
AU Hirst D.G.; **Denekamp J.**; Hobson B.
CS Gray Lab., Mt. Vernon Hosp., Northwood, Middlesex, HA6 2RN, United Kingdom
SO Cell and Tissue Kinetics, (1982) 15/3 (251-261).
CODEN: CTKIAR
CY United Kingdom
DT Journal
FS 016 Cancer
023 Nuclear Medicine
005 General Pathology and Pathological Anatomy
LA English

L5 ANSWER 7 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82045712 EMBASE
DN 1982045712
TI **Endothelial** cell proliferation as a novel approach to targeting tumor therapy.
AU **Denekamp J.**
CS Gray Lab. Cancer Res. Campaign, Mount Vernon Hosp., Northwood, Middlesex HA6 2RN, United Kingdom
SO British Journal of Cancer, (1982) 45/1 (136-139).
CODEN: BJCAAI
CY United Kingdom
DT Journal
FS 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
013 Dermatology and Venereology
LA English